

Knowledge of medication-related osteonecrosis of the jaw among dental and medical students in Riyadh, Saudi Arabia: A comparative study

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Author Affiliation:

¹College of Dentistry, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia

²King Abdullah International Medical Research Center, Riyadh, Saudi Arabia; Email: khindap@ksau-hs.edu.sa, saeedsa@ksau-hs.edu.sa

³Preventive Dental Science Department, College of Dentistry, King Saud bin Abdulaziz University for health Sciences, Riyadh, Saudi Arabia

⁴Maxillofacial Surgery and Diagnostic Science Department, College of Dentistry, King Saud bin Abdulaziz University for health Sciences, Riyadh, Saudi Arabia

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Paramjit Kaur Khinda^{1,2,3}, Safa Saeed^{1,2,4}, Salem Alshanbari¹, Adeeb Alshareef¹, Mohammed Matrood¹, Khalid Alothman¹, Abdulrahman Alqarni¹, Khalid Alshehri¹

ABSTRACT

Objectives: To assess and compare the knowledge of dental and medical students about medication-related osteonecrosis of the jaw (MRONJ).

Materials and Methods: This cross-sectional study consisting of a questionnaire was conducted among dental and medical students in their fifth and sixth year of study in various colleges in Riyadh, Saudi Arabia. Data was collected online by a self-reported questionnaire consisting of close ended and multiple-choice questions. Chi-square test was performed; the significant level was found to be $p < 0.05$. **Results:** A total of 352 dental and medical students participated in the survey. 65.4% of the respondents stated that they were familiar with the term MRONJ, yet less than 45% were aware of the risk factors, clinical appearance, and features of the disease. During the time that three-fourths of the respondents acknowledged the importance of recording BPs history, a greater number did not know the accurate treatment approach. Students in the sixth year had better knowledge than fifth-year students and dental students fared better than medical students. **Conclusion:** If it is initiatives such as workshops and lectures need to be started to broaden the knowledge of medical as well as dental students which will contribute to the prevention of MRONJ.

Keywords: bisphosphonates, bone, dentists, jaw, osteonecrosis, knowledge, dental practitioners, Bisphosphonate-related osteonecrosis of the jaw, medication-related osteonecrosis of the jaw, oral pathology

1. INTRODUCTION

The bisphosphonates (BPs) are a class of drugs having affinity for bone tissue, leading to inhibition resolution of bone resorption by inhibiting the

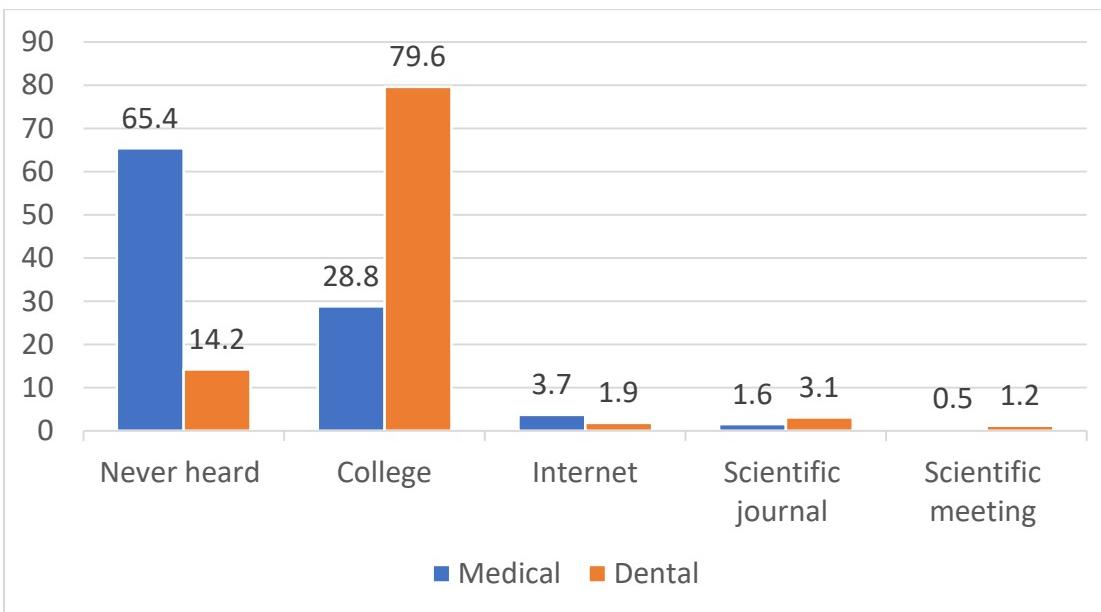
osteoclastic activity (Rosella et al., 2017; Al-Maweri et al., 2020). The BPs reduce bone turnover by their anti-osteoclastic as well as antiangiogenic activity (De Lima et al., 2015). BPs are widely used in the treatment of osteoporosis and metabolic bone disease as well as the management of skeletal complications of malignancy (López-jornet et al., 2010; Franchi et al., 2020). It is estimated that the incidence of bisphosphonate related osteonecrosis of the jaw (BRONJ) in patients with malignancies ranges between 1 to 10% (Franchi et al., 2020; Tanna et al., 2017; Ruggiero et al., 2014). There are other antiresorptive drugs besides BPs that can lead to osteonecrosis of the jaw, therefore, the nomenclature was changed to medication related osteonecrosis of the jaw (MRONJ) by the American Association of Maxillofacial Surgeons (AAOMS) in 2014 (Ruggiero et al., 2014). MRONJ is a severe negative drug response which consists of increasing bone destruction in the maxillofacial area of patients (Coleman, 2008). Patients must undergo detailed dental evaluation before initiating treatment with BPs and related drugs, so that the occurrence of MRONJ is prevented (Reid, 2009). In order to effectively treat patients receiving bisphosphonates and related drugs, dental and medical students must know these drugs and their possible adverse effects, so that any complications can be avoided. To the best of our knowledge, no study has assessed and compared the dental and medical students' knowledge regarding MRONJ in Riyadh, Saudi Arabia. Hence this study was designed to evaluate the knowledge of dental and medical students about MRONJ in order to optimize the future training programs in this important field.

2. METHODOLOGY

This cross-sectional study consisting of a questionnaire was conducted among dental and medical students in their fifth and sixth years of study in various colleges in Riyadh, Saudi Arabia. The research was reviewed and approved under reference #SP20-498-R from the Institutional Review Board (IRB) of the King Abdullah International Medical Research Center (KAIMRC) prior to the commencement of the study. The questionnaire was prepared after referring to pre validated questionnaires used in similar studies (Coleman, 2008; Abu-id et al., 2008; Edwards et al., 2008). The collection of data was done between September 2020 and December 2020. The questionnaire consisted of two parts, first part related to general information including age, gender, and year of study. The second part focused on assessment of general knowledge, risk factors, clinical features and prevention and management of medication related osteonecrosis of the jaw. A cluster random sample technique was selected. Considering each college, a cluster, the sample was selected randomly from each cluster. Prior to the participation, all subjects were required to fill a consent form and the information provided by the participants was kept confidential. The study was reviewed by King Abdullah International Medical Centre and approved by its ethical committee.

3. RESULTS

A total of 363 dental and medical students in their fifth and sixth years of study participated in the survey. After excluding the incomplete responses, the sample size was 352. Among the participants, 188 were males (53.40%) and 164 were females (46.60%). The mean age of the participants was 22.67, while the median age was 24. Of the 352 students, 191 were medical students (54.26%), and 161 were dental students (45.74%). 5th year (medical and dental) students were 189 (53.70%) while 6th year students were 163 (46.30%). Table 1 presents the general knowledge of participants about MRONJ. Around 56.4 % of the respondents were familiar with the term MRONJ, with significant differences among dental (83.5%) and medical (33.5%) students and between male (46.8%) and female (67.3%) students (Figure 1). Participants were asked if patient should be asked about BPs usage, 73.1 % of total respondents agreed that it was important with significant difference between dental (87.7%) and medical students (60.7 %). Regarding the question, if BPs and some other drugs can lead to ONJ, 57.2 % of total respondents answered correctly with significant difference between dental (80.9 %) and medical students (37.2 %), and among male (48.9 %) and female (66.7 %) students. 25.8 % of the respondents reported to be familiar with the disease staging and treatment guidelines suggested by AAOMS, with a significant difference among dental (44.4%) and medical (9.9%) students.

**Figure 1** Source of information regarding MRONJ percentage**Table 1** General knowledge about MRONJ (% of the correct answer)

	Total	Major			Gender			Years of study		
		Dental	Medical	p-Value	M	F	p-Value	5	6	p-Value
Familiar with MRONJ	56.4	83.3	33.5	0.000	46.8	67.3	0.000	51.9	61.6	0.066
Asking if PT is using BP	73.1	87.7	60.7	0.000	69.1	77.6	0.110	73	73.2	0.994
Do you know that BPs and some other drugs can lead to ONJ	57.2	80.9	37.2	0.000	48.9	66.7	0.004	54	61	0.367
Familiarity with AAOMS guidelines and treatment strategies	25.8	44.4	9.9	0.000	19.1	33.3	0.002	20.6	31.7	0.018

Table 2 presents students' knowledge regarding bisphosphonates and other drugs beside BPs that can lead to MRONJ. Most known bisphosphonate was alendronate (32.1%) with no significant difference among dental and medical students and among males and females. The highest known drug beside BPs was denosumab (21.1 %) with significant difference between dental (26.5%) and medical (15.7%) as well as sixth (32.9%)and fifth year students (10.9%).71.3% did not know about drugs other than BPs, that can cause MRONJ.

Table 2 knowledge about BP drugs and other drugs beside BP (% of the correct answer)

Types of BP**	Total	Major			Gender			Year of study		
		Dental	Medical	p-Value	M	F	p-Value	5	6	p-Value
Alendronate (Fosamax)	32.1	28.4	35.1	0.180	33.5	30.3	0.519	23.3	42.1	0.000
Risendronate (Actonel)	19.1	15.4	22.0	0.117	16.5	21.8	0.203	13.8	25.0	0.007
Ibandronate (Boniva)	16.2	13.6	18.3	0.227	16	16.4	0.918	13.8	18.9	0.190
Zolendronate (Zometa)	20.1	19.3	20.5	0.766	19.8	20.1	0.937	16.5	23.9	0.082
Neridronate	7.4	8.0	6.8	0.662	6.9	7.9	0.729	5.8	9.1	0.233

Pamidronate	11.1	11.1	11.1	0.986	11.8	10.3	0.663	8.5	14.0	0.010
Tiludronate	10.3	11.7	8.9	0.382	11.2	9.1	0.520	6.3	14.6	0.010
IDK	60.8	64.2	58.1	0.243	59	63	0.444	68.8	51.8	0.001

Table 2 (continued)

Drugs besides BPs	Total	Major			Gender			Year of study		
		Dental	Medical	p-Value	M	F	p-Value	5	6	p-Value
Denosumab	21.1	26.5	15.7	0.012	21.8	19.4	0.576	10.1	32.9	0.000
Sunitinib	3.2	4.9	1.6	0.70	4.3	1.8	0.189	0.5	6.1	0.003
Sorafenib	3.2	5.6	1	0.015	3.2	3	0.931	1.6	4.9	0.076
Bevacizumab	5.4	7.4	3.7	0.121	4.8	6.1	0.597	4.8	6.1	0.579
Sirolimus	5.5	11.1	0.5	0.000	7.4	3.0	0.067	2.1	9.1	0.004
IDK	73.1	65.2	80.6	0.001	71.8	75.6	0.420	83.5	62.2	0.000

Table 3 presents dental and medical students' knowledge regarding risk factors and clinical features of MRONJ. Regarding risk factors for MRONJ, the correct answers ranged from 4.4 to 34 %. The most identified risk factors were tobacco use (34%), duration of therapy (33.8%), steroid therapy (18.7%), and route of administration (15.4%). 41.3% were unaware of risk factors. Similarly, the students' knowledge regarding clinical features of the disease ranged from 14.3% to 44.8%. There was a significant difference between dental and medical students regarding route of administration and antibiotic therapy. Pain (44.8%) was the most well-known clinical feature of MRONJ followed by pathologic fracture (35.8%). Next, participants were asked for the pathologies for which BPs are used. Percentage of correct answers ranged from 11.1 to 40.4%, with the most identified pathologies as osteopenia and osteopetrosis (40.4%), followed by Paget's disease (26.3 %) with no significant difference among dental and medical students and between males and females (table 4).

Table 3 Knowledge regarding risk factors and clinical features of MRONJ (% of correct answers [Yes answers])

Items	Total	Major			Gender			Year of study		
		Dental	Medical	p-Value	M	F	p-Value	5	6	p-Value
Risk factors										
Route of administration	15.4	22.2	8.9	0.000	10.6	20	0.014	10.6	20.1	0.012
Arterial hypertension	4.4	3.7	5.2	0.491	4.8	4.2	0.806	6.3	2.4	0.078
Antibiotic therapy	5.8	9.3	2.6	0.008	6.4	4.9	0.535	4.2	7.4	0.201
Tobacco use	34	34.0	34	0.987	37.2	30.3	0.170	32.8	35.4	0.612
Steroid therapy	18.7	19.1	18.3	0.846	16.5	21.2	0.256	20.1	17.1	0.466
Hyperlipidemia	2.8	2.5	3.1	0.704	2.7	3	0.834	4.8	0.6	0.019
Alcohol	14.8	16.7	13.1	0.345	15.4	13.9	0.694	12.7	17.1	0.247
Microtrauma	11.4	11.1	11.5	0.904	11.2	11.5	0.919	9.5	13.4	0.250
Duration of therapy	33.8	45.1	23.0	0.000	25	42.4	0.001	28.6	38.4	0.050
IDK	41.3	31.5	50.3	0.000	43.6	39.4	0.422	45.5	37.2	0.050

Table 3 (continued)

Clinical featured of MRONJ	Total	Major			Gender			Year of study		
		Dental	Medical	p-Value	M	F	p-Value	5	6	p-Value
Pain	44.8	49.4	40.3	0.088	43.1	46.1	0.575	37.6	52.4	0.005
Purulent discharge	19.1	18.6	13.6	0.199	14.9	17.1	0.577	13.2	19.0	0.139
Expose bone	30.8	65.4	11.5	0.000	33.5	39.4	0.251	24.9	49.4	0.000
fistula	14.4	21.6	7.9	0.000	16.0	12.1	0.302	7.9	21.3	0.000
Paresthesia	14.3	22.2	7.4	0.000	13.8	14.6	0.829	15.4	12.8	0.482
Pathologic fracture	35.8	38.9	33.0	0.249	34.0	37.6	0.489	32.8	39.0	0.244
IDK	41.2	25.3	56.0	0.000	45.2	38.2	0.182	49.2	33.5	0.003

The BPs is used in the treatment of which of the following pathologies?	Total	Major			Gender			Year of study		
		Dental	Medical	p-Value	M	F	p-Value	5	6	p-Value
Bone metastasis	19.6	30.9	9.4	0.000	16.0	23.0	0.093	17.5	21.3	0.356
Osteomyelitis	14.5	25.3	4.7	0.000	14.4	13.9	0.910	12.2	16.5	0.248
Multiple myeloma	11.1	17.9	4.7	0.000	8.5	13.4	0.139	7.4	14.7	0.027
Hypercalcemia of malignancy	13.8	13.0	14.7	0.646	14.4	13.3	0.780	13.2	14.6	0.703
Osteopetrosis	39.7	43.2	36.6	0.209	41.0	38.2	0.595	40.2	39.0	0.820
Osteopenia and osteopetrosis	40.4	39.1	41.1	0.714	41.5	38.7	0.588	28.7	53.4	0.000
Paget's disease	26.3	30.9	22.1	0.062	26.6	25.5	0.807	21.7	31.1	0.045
IDK	26.6	23.5	29.8	0.178	28.7	24.8	0.413	31.7	21.3	0.028

Table 4 Knowledge regarding dental therapy/preventive strategies in patients undergoing BP treatment (% of the correct answer)

	Total	Major			Gender			Year of study		
		Dental	Medical	P-Value	M	F	P-Value	5	6	P-Value
Patients to be checked by a dentist before IV BP treatment? (correct answer: Yes)	62.8	77.8	50	0.000	56.1	70.3	0.011	57.7	68.7	0.100
Invasive dental treatment during IV BP therapy? (correct answer: No)	39.3	63.4	18.9	0.000	29.6	50.3	0.000	32.8	46.9	0.022
Dental treatment in patients with oral BP therapy for < 4 years without risk factors? (correct answer: Yes)	8.8	11.7	6.3	0.000	8	9.7	0.033	7.9	9.8	0.011

Invasive dental treatment during oral BP therapy for < 4 years with risk factors? (correct answer: No)	12.8	20.4	6.3	0.000	10.2	15.8	0.094	9	17.2	0.033
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4. DISCUSSION

Many case series of MRONJ have been published in the literature. Moreover, the frequency of new cases being described in the literature is increasing. Since this is an area common to both dental and medical specialities, knowledge regarding this should be imparted to both dental and medical students. To the best of our knowledge, this is the only cross-sectional study designed to assess and compare the knowledge of medical and dental students regarding MRONJ. The mean age of the participants in this study was (22.7), which is almost similar to a study conducted in Italy (Rosella et al., 2017), with mean age of (24.1). The number of male respondents in this study was 188 (53.3%). In contrast, the male respondents in the study by (Rosella et al., 2017) were (44.9%). The male respondents in a study conducted in Saudi Arabia (Al-Maweri et al., 2020) dentists were 66.4%. Moreover, the numbers of participants in their 6th year of study were 164 (46.5%). This was similar to a study done among dental students in Brazil (De Lima et al., 2015) (49%).

In the present study, only (56.4%) of the respondents had heard about MRONJ. In a study conducted in Saudi Arabia (Al-Maweri et al., 2020) on dentists, (71%) of participants were familiar with MRONJ. Dental school was the main source of information regarding MRONJ in our study (52.1%) compared to other sources. This was similar to the study by (Al-Maweri et al., 2020) in which 49% of the respondents gained the information about MRONJ from dental school (Al-Eid et al., 2020). In our study, (73.1%) of participants acknowledged the importance of asking patients if they were undergoing BP treatment. This was similar to the study done by (Al-Maweri et al., 2020) who reported that (70.4%) of dentists acknowledged the importance of asking patients if they were undergoing BP treatment. This contrasts with a study done by (Rosella et al., 2017) in which (93.9%) dental students responded positively to the same question. The participants were asked if they are updated with staging guidelines and treatment strategies suggested by American Association of Oral and Maxillofacial Surgeons (AAOMS). Only (25.8%) of participants were familiar with the guidelines. This was similar to study by (Al-Maweri et al., 2020) in which (36.4%) of the total participants were aware of the guidelines.

In the present study the most known diseases were osteopenia/osteoporosis (40.9%), and osteopetrosis (39.9%) respectively. Similarly, osteopenia/osteoporosis was the most known diseases (57.5%) in the study by (Al-Maweri et al., 2020). Also, osteopenia/osteoporosis scored the highest in (Rosella et al., 2017) study. Moreover, the most well-known drug was alendronate (32%). Also, alendronate was the most recognized drug (35.1%) in (Al-Maweri et al., 2020) study. However, zoledronate was the most known in (Rosella et al., 2017) (71.4%) study. Next, participants were asked regarding other drugs that can lead to MRONJ besides BPs and denosumab was recognized as the most known drug besides BPs (21.1%). Denosumab was also the highest recognized drug in the study done by (Rosella et al., 2017) (29.6%). In comparison to a study conducted in London by (Tanna et al., 2017), only (2%) of the respondents were aware of denosumab. Regarding the risk factors of MRONJ, the highly recognized risk factors were tobacco and duration of therapy (34%). Comparatively, in study by (Rosella et al., 2017), the most recognized risk factor was duration of therapy (79.6%) followed by way of administration (71.4%) in (Al-Maweri et al., 2020) study, the risk factors that were most recognized were type of BP therapy (67.1%) followed by dentoalveolar surgery (55.4%). Regarding clinical features of MRONJ, pain was the most known (44.9%) followed by exposed bone (38.5%). This was similar to the study by (Al-Maweri et al., 2020) who also reported exposed bone (64.9%) and pain (61.9%) as the most common.

When asked whether patients should be checked by dental practitioner before starting intravenous (IV) BPs, (62.8%) agreed that the patient should be checked while (7.7%) responded negatively while (29.5%) said that they did not know. The majority of participants in (Rosella et al., 2017) study agreed on the need for a check-up (81.6%). Comparatively, in the study conducted by (Al-Maweri et al., 2020), the percentage of participants responding positively was (71.7%). Also, in a study conducted in Spain (López-jornet et al., 2010) the percentage of positive response was (95%). Surprisingly, only (58.1%) either agreed or strongly agreed in the study by (Al-Eid et al., 2020). Lastly, in a study surveying medical students conducted in Italy by (FranchI et al., 2020) (98.6%) of respondents answered positively.

In our study, 53.3% of the participants did not know if invasive dental treatment could be provided to those undergoing IV BP treatment, 39.3 % said that dental treatment should not be carried out, and only 7.4% answered yes. However, (80.6%) knew that it should not be carried out in (Rosella et al., 2017) study. Whereas (51.6%) of participants answered correctly in (Al-Maweri et al., 2020) study. Next, participants were questioned whether dental treatment can be provided to patients using oral BPs for a period of less than 4 years without risk factors. Only (8.8%) of respondents knew that dental treatment can be provided while (23.3%)

believed that dental treatment cannot be provided, and (67.9%) did not know. In (Rosella et al., 2017) study, the participants who answered correctly was (33.7%). Likewise, (40.5%) in (Al-Maweri et al., 2020) study knew the correct answer. Finally, participants were questioned whether dental treatment can be provided to patients using oral BPs for a period of less than 4 years with risk factors. Only (12.8%) knew that dental treatment should not be carried out in this case, (22.7%) said that dental treatment can be carried out and (64.5%) did not know. In (Rosella et al., 2017) study, the percentage of correct answers was (23.5%). Similarly, (34.6%) in (Al-Maweri et al., 2020) study knew the correct answer. It can be inferred from this study that there is a lack of knowledge among dental as well as medical students regarding MRONJ.

The limitation of this study is that it being a cross sectional survey done in Riyadh, cannot be generalized to entire country. It is therefore suggested that similar studies be carried out in other parts of the country.

5. CONCLUSION

In conclusion, similar to previous studies in other countries, this study revealed poor knowledge about MRONJ among dental and medical students in their last two clinical years in Riyadh, Saudi Arabia. However, dental students had better knowledge regarding MRONJ than medical students. These results necessitate actions to improve medical and dental students' knowledge and awareness about MRONJ and the importance of following the established guidelines for treatment of population at risk of MRONJ. Conducting periodic continuing education courses and workshops related to MRONJ is the answer to address this obvious gap in the knowledge about MRONJ and to implement these guidelines.

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Author Contributions

All authors contributed to the design and implementation of the research, to the analysis of the research and to the writing of the manuscript

Ethical approval

The research was reviewed and approved under reference #SP20-498-R from the Institutional Review Board (IRB) of the King Abdullah International Medical Research Center (KAIMRC).

Conflicts of interest

The authors declare that they have no conflict of interest.

Funding

This study has not received any external funding.

Data and materials availability

All data associated with this study are present in the paper.

Appendix A

Domain 1: Demographic data

Age: 1.1

Gender: 1.2

A. Male

B. Female

1.3: Major

A. Medical student

B. Dental student

1.4: Year of study

C. 5th year

D. 6th year (last year before internship)

Domain 2: General knowledge

2.1: Are you familiar with the term MRONJ?

A. Yes

B. No

2.2: From where did you learn about MRONJ for the first time?

A. Never heard

B. College

C. Internet

D. Scientific Journals

E. Scientific meeting

2.3: Do you think it is important to ask if patients are using bisphosphonates?

A. Yes

B. No

C. I don't know

2.4: Do you know that bisphosphonates and some other drugs can lead to osteonecrosis of the jaw (ONJ)?

A. Yes

B. No

C. I don't know

2.5: Are you familiar with bisphosphonates-related osteonecrosis staging guidelines and treatment strategies suggested by American Association of Oral and Maxillofacial Surgeons (AAOMS)?

A. Yes

B. No

2.6: The bisphosphonates are used in the treatment of which of the following pathologies? (It is possible to mark more than one choice)

A. Bone metastasis

B. Osteomyelitis

C. Multiple myeloma

D. Hypercalcemia of malignancy

E. Osteopetrosis

F. Osteopenia and osteoporosis

G. Paget's disease of bone

H. I don't know

2.7: Which of the following belong to bisphosphonates group of drugs? (It is possible to mark more than one answer)

A. Alendronate

B. Risedronate

C. Ibandronate

D. Neridronate

E. Pamidronate

F. Zoledronate

G. Tiludronate

H. I don't know

2.8: Which of the following drugs may cause osteonecrosis of the jaw besides bisphosphonates? (It is possible to mark more than one answer)

A. Denosmab

B. Sunitinib

C. Sorafenib

D. Bevacizumab

E. Sirolimus

F. I don't know

Domain 3: Risk factor

3.1: What are the risk factors related to osteonecrosis of the jaw? (It is possible to mark more than one choice)

- A. Tobacco
- B. Antibiotic therapy
- C. Route of administration
- D. Alcohol
- E. Arterial hypertension
- F. Duration of therapy
- G. Hyperlipidemia
- H. Steroid therapy
- I. Microtrauma
- J. I don't know

Domain 4: Clinical features

4.1: which of the following are the clinical features of MRONJ? (It is possible to mark more than one choice)

- A. Pain
- B. Purulent discharge
- C. Exposed bone
- D. Fistula
- E. Paresthesia
- F. Pathologic fracture
- G. I don't Know

Domain 5: Prevention and management

5.1: Do you think patients should be checked by the dentist before the start of treatment with intravenous bisphosphonates treatment?

- A. Yes
- B. No
- C. I don't know

5.2: Can invasive dental treatments be given to patients during an intravenous bisphosphonate drug therapy?

- A. Yes
- B. No
- C. I don't know

5.3: Can invasive dental treatments be given to patients using oral bisphosphonates for a period of less than 4 years WITHOUT risk factors?

- A. Yes
- B. No
- C. I don't know

5.4: Can invasive dental treatments be given to patients using oral bisphosphonates for a period of less than 4 years WITH risk factors?

- A. Yes
- B. No
- C. I don't know

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